

WE CLAIM:

1. A method of detecting a nucleic acid having at least two portions comprising:

providing a type of nanoparticles having oligonucleotides attached thereto, the oligonucleotides on each nanoparticle having a sequence complementary to the sequence of at least two portions of the nucleic acid;

contacting the nucleic acid and the nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the two or more portions of the nucleic acid; and

observing a detectable change brought about by hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

2. A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with at least two types of nanoparticles having oligonucleotides attached thereto, the oligonucleotides on the first type of nanoparticles having a sequence complementary to a first portion of the sequence of the nucleic acid, the oligonucleotides on the second type of nanoparticles having a sequence complementary to a second portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the nucleic acid; and

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observing a detectable change brought about by hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

3. The method of Claim 2 wherein the contacting conditions include freezing and thawing.

4. The method of Claim 2 wherein the contacting conditions include heating.

5. The method of Claim 2 wherein the detectable change is observed on a solid surface.

6. The method of Claim 2 wherein the detectable change is a color change observable with the naked eye.

7. The method of Claim 6 wherein the color change is observed on a solid surface.

8. The method of Claim 2 wherein the nanoparticles are made of gold.

9. The method of Claim 2 wherein the oligonucleotides attached to the nanoparticles are labelled on their ends not attached to the nanoparticles with molecules that produce a detectable change upon hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

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10. The method of Claim 9 wherein the nanoparticles are metallic or semiconductor nanoparticles and the oligonucleotides attached to the nanoparticles are labeled with fluorescent molecules.

11. The method of Claim 2 wherein:

the nucleic acid has a third portion located between the first and second portions, and the sequences of the oligonucleotides on the nanoparticles do not include sequences complementary to this third portion of the nucleic acid; and

the nucleic acid is further contacted with a filler oligonucleotide having a sequence complementary to this third portion of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the filler oligonucleotide with the nucleic acid.

12. The method of Claim 2 wherein the nucleic acid is viral RNA or DNA.

13. The method of Claim 2 wherein the nucleic acid is a gene associated with a disease.

14. The method of Claim 2 wherein the nucleic acid is a bacterial DNA.

15. The method of Claim 2 wherein the nucleic acid is a fungal DNA.

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16. The method of Claim 2 wherein the nucleic acid is a synthetic DNA, a synthetic RNA, a structurally-modified natural or synthetic RNA, or a structurally-modified natural or synthetic DNA.

17. The method of Claim 2 wherein the nucleic acid is from a biological source.

18. The method of Claim 2 wherein the nucleic acid is a product of a polymerase chain reaction amplification.

19. The method of Claim 2 wherein the nucleic acid is contacted with the first and second types of nanoparticles simultaneously.

20. The method of Claim 2 wherein the nucleic acid is contacted and hybridized with the oligonucleotides on the first type of nanoparticles before being contacted with the second type of nanoparticles.

21. The method of Claim 20 wherein the first type of nanoparticles is attached to a substrate.

22. The method of Claim 2 wherein the nucleic acid is double-stranded and hybridization with the oligonucleotides on the nanoparticles results in the production of a triple-stranded complex.

contacting the nucleic acid bound to the substrate with the second type of nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the second type of nanoparticles with the nucleic acid; and observing a detectable change.

24. The method of Claim 23 wherein the nanoparticles are made of gold.

providing a substrate having a first type of nanoparticles attached thereto, the nanoparticles having oligonucleotides attached thereto, the oligonucleotides

having a sequence complementary to a first portion of the sequence of the nucleic acid;

contacting the nucleic acid with the nanoparticles attached to the substrate under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the nucleic acid;

providing a second type of nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to one or more other portions of the sequence of the nucleic acid;

contacting the nucleic acid bound to the substrate with the second type of nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the second type of nanoparticles with the nucleic acid;

providing a binding oligonucleotide having a selected sequence having at least two portions, the first portion being complementary to at least a portion of the sequence of the oligonucleotides on the second type of nanoparticles;

contacting the binding oligonucleotide with the second type of nanoparticles bound to the substrate under conditions effective to allow hybridization of the binding oligonucleotide to the oligonucleotides on the nanoparticles;

providing a third type of nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to the sequence of a second portion of the binding oligonucleotide;

observing a detectable change.

27. The method of Claim 26 wherein the detectable change is the formation of dark areas on the substrate.

28. The method of Claim 25 wherein the nanoparticles are made of gold.

29. A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with the nucleic acid;

contacting the nucleic acid bound to the substrate with a first type of nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to one or more other portions of the sequence

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31. The method of Claim 30 wherein the detectable change is the formation of dark areas on the substrate.

32. The method of Claim 29 wherein the nanoparticles are made of gold.

33. A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of the nucleic acid, the contacting



taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with the nucleic acid;

contacting the nucleic acid bound to the substrate with liposomes having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the liposomes with the nucleic acid;

contacting the liposomes bound to the substrate with a first type of nanoparticles having at least a first type oligonucleotides attached thereto, the first type of oligonucleotides having a hydrophobic group attached to the end not attached to the nanoparticles, the contacting taking place under conditions effective to allow attachment of the oligonucleotides on the nanoparticles to the liposomes as a result of hydrophobic interactions; and

observing a detectable change.

34. A method of detecting nucleic acid having at least two portions comprising

contacting the nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with the nucleic acid;

contacting the nucleic acid bound to the substrate with liposomes having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the liposomes with the nucleic acid;

contacting the liposomes bound to the substrate with a first type of nanoparticles having at least a first type oligonucleotides attached thereto, the first type of oligonucleotides having a hydrophobic group attached to the end not attached to the nanoparticles, the contacting taking place under conditions effective to allow attachment of the oligonucleotides on the nanoparticles to the liposomes as a result of hydrophobic interactions;

contacting the first type of nanoparticles bound to the liposomes with a second type of nanoparticles having oligonucleotides attached thereto,

the first type of nanoparticles having a second type of oligonucleotides attached thereto which have a sequence complementary to at least a portion of the sequence of the oligonucleotides on the second type of nanoparticles,

the oligonucleotides on the second type of nanoparticles having a sequence complementary to at least a portion of the sequence of the second type of oligonucleotides on the first type of nanoparticles,

the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and observing a detectable change.

35. A method of detecting a nucleic acid having at least two portions comprising:

providing nanoparticles having oligonucleotides attached thereto;

providing one or more types of binding oligonucleotides, each of the binding oligonucleotides having two portions, the sequence of one portion being complementary to the sequence of one of the portions of the nucleic acid and the sequence of the other portion being complementary to the sequence of the oligonucleotides on the nanoparticles;

contacting the nanoparticles and the binding oligonucleotides under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the binding oligonucleotides;

contacting the nucleic acid and the binding oligonucleotides under conditions effective to allow hybridization of the binding oligonucleotides with the nucleic acid; and

observing a detectable change.

36. The method of Claim 35 wherein the nanoparticles are contacted with the binding oligonucleotides prior to being contacted with the nucleic acid.

37. A method of detecting a nucleic acid having at least two portions comprising:

providing nanoparticles having oligonucleotides attached thereto;

providing one or more binding oligonucleotides, each of the binding oligonucleotides having two portions, the sequence of one portion being complementary to the sequence of at least two portions of the nucleic acid and the sequence of the other portion being complementary to the sequence of the oligonucleotides on the nanoparticles;

contacting the nanoparticles and the binding oligonucleotides under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the binding oligonucleotides;

contacting the nucleic acid and the binding oligonucleotides under conditions effective to allow hybridization of the binding oligonucleotides with the nucleic acid; and

observing a detectable change.

38. A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with at least two types of particles having oligonucleotides attached thereto,

the oligonucleotides on the first type of particles having a sequence complementary to a first portion of the sequence of the nucleic acid and being labeled with an energy donor,

the oligonucleotides on the second type of particles having a sequence complementary to a second portion of the sequence of the nucleic acid and being labeled with an energy acceptor,

the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the particles with the nucleic acid; and

observing a detectable change brought about by hybridization of the oligonucleotides on the particles with the nucleic acid.

39. The method of Claim 38 wherein the energy donor and acceptor are fluorescent molecules.

40. A method of detecting nucleic acid having at least two portions comprising:

providing a type of latex microspheres having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of the nucleic acid and being labeled with a fluorescent molecule;

providing a type of gold nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a second portion of the sequence of the nucleic acid;

contacting the nucleic acid with the latex microspheres and the nanoparticles under conditions effective to allow hybridization of the oligonucleotides on

observing changes in fluorescence, color or both.

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A method of detecting nucleic acid having  
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providing a second type of metallic or  
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the oligonucleotides having a sequence  
complementary to a second portion of the sequence of  
the nucleic acid and being labeled with a fluorescent  
dye;  
contacting the nucleic acid with the two  
nanoparticles under conditions effective to allow  
hybridization of the oligonucleotides on the two  
nanoparticles with the nucleic acid; and  
observing changes in fluorescence.

contacting the nucleic acid with the two types of nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the two types of nanoparticles with the nucleic acid; and

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43. The method of Claim 42 further comprising placing a portion of the mixture of the nanoparticles and nucleic acid in an observation area located on a microporous material, treating the microporous material so as to remove any unbound nanoparticles from the observation area, and then observing the changes in fluorescence.

44. A method of detecting nucleic acid having at least two portions comprising:

providing a type of particle having oligonucleotides attached thereto, the oligonucleotides having a first portion and a second portion, both portions being complementary to portions of the sequence of the nucleic acid;

providing a type of probe oligonucleotides comprising a first portion and a second portion, the first portion having a sequence complementary to the first portion of the oligonucleotides attached to the particles and both portions being complementary to portions of the sequence of the nucleic acid, the probe oligonucleotides further being labeled with a reporter molecule at one end;

contacting the particle and the probe oligonucleotides under conditions effective to allow for hybridization of the oligonucleotides on the particles with the probe oligonucleotides to produce a satellite probe;

then contacting the satellite probe with the nucleic acid under conditions effective to provide for hybridization of the nucleic acid with the probe oligonucleotides;

particles; and

a reporter molecule.

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50. The kit of Claim 48 wherein the nanoparticles are made of gold.

51. The kit of Claim 48 further comprising a solid surface.

52. A kit comprising at least two containers,  
the first container holding nanoparticles having oligonucleotides attached thereto which have a sequence complementary to the sequence of a first portion of a nucleic acid, and

the second container holding nanoparticles having oligonucleotides attached thereto which have a sequence complementary to the sequence of a second portion of the nucleic acid.

53. The kit of Claim 52 comprising a third container holding oligonucleotides having a sequence complementary to a third portion of the nucleic acid, the third portion being located between the first and second portions.

54. The kit of Claim 52 wherein the nanoparticles are made of gold.

55. The kit of Claim 52 further comprising a solid surface.

56. A kit comprising at least two containers,

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the first container holding nanoparticles having oligonucleotides attached thereto which have a sequence complementary to the sequence of a first portion of a binding oligonucleotide, and

the second container holding one or more types of binding oligonucleotides, each of which has a sequence comprising at least two portions, the first portion being complementary to the sequence of the oligonucleotides on the nanoparticles and the second portion being complementary to the sequence of a portion of a nucleic acid.

57. The kit of Claim 56 which comprises additional containers, each holding an additional binding oligonucleotide, each additional binding oligonucleotide having a sequence comprising at least two portions, the first portion being complementary to the sequence of the oligonucleotides on the nanoparticles and the second portion being complementary to the sequence of another portion of the nucleic acid.

58. The kit of Claim 56 wherein the nanoparticles are made of gold.

59. The kit of Claim 56 further comprising a solid surface.

60. A kit comprising:  
a container holding one type of nanoparticles having oligonucleotides attached thereto and one or more

types of binding oligonucleotides, each of the types of binding oligonucleotides having a sequence comprising at least two portions, the first portion being complementary to the sequence of the oligonucleotides on the nanoparticles, whereby the binding oligonucleotides are hybridized to the oligonucleotides on the nanoparticles, and the second portion being complementary to the sequence of one or more portions of a nucleic acid.

61. A kit comprising at least one container, the container holding metallic or semiconductor nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a portion of a nucleic acid and having fluorescent molecules attached to the ends of the oligonucleotides not attached to the nanoparticles.

62. A kit comprising:

a substrate, the substrate having attached thereto nanoparticles, the nanoparticles having oligonucleotides attached thereto which have a sequence complementary to the sequence of a first portion of a nucleic acid; and

a first container holding nanoparticles having oligonucleotides attached thereto which have a sequence complementary to the sequence of a second portion of the nucleic acid.

63. The kit of Claim 62 further comprising:

a third container holding nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to the sequence of a second portion of the binding oligonucleotide.

65. The kit of Claim 64 further comprising a fourth container holding a third oligonucleotide having a sequence complementary to the sequence of a third portion of the nucleic acid, the third portion being located between the first and second portions.

66. The kit of Claim 64 further comprising a substrate.

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a fifth container holding an oligonucleotide having a sequence complementary to the sequence of a second portion of the binding oligonucleotide.

69. The kit of Claim 66 wherein the substrate, nanoparticles, or both bear functional groups for attachment of the nanoparticles to the substrate.

71. The kit of Claim 64 wherein the nanoparticles are made of gold.

72. A kit comprising:  
a substrate having oligonucleotides attached thereto which have a sequence complementary to the sequence of a first portion of a nucleic acid;  
a first container holding nanoparticles having oligonucleotides attached thereto, some of which have a

sequence complementary to the sequence of a second portion of the nucleic acid; and

a second container holding nanoparticles having oligonucleotides attached thereto which have a sequence complementary to at least a portion of the sequence of the oligonucleotides attached to the nanoparticles in the first container.

73. A kit comprising:

a substrate;

a first container holding nanoparticles;

a second container holding a first oligonucleotide having a sequence complementary to the sequence of a first portion of a nucleic acid;

a third container holding a second oligonucleotide having a sequence complementary to the sequence of a second portion of the nucleic acid; and

a fourth container holding a third oligonucleotide having a sequence complementary to at least a portion of the sequence of the second oligonucleotide.

74. The kit of Claim 73 wherein the oligonucleotides, nanoparticles, substrate or all bear functional groups for attachment of the oligonucleotides to the nanoparticles or for attachment of the oligonucleotides to the substrate.

75. The kit of Claim 73 wherein the nanoparticles are made of gold.

76. A kit comprising:

a substrate having oligonucleotides attached thereto which have a sequence complementary to the sequence of a first portion of a nucleic acid;

a first container holding liposomes having oligonucleotides attached thereto which have a sequence complementary to the sequence of a second portion of the nucleic acid; and

a second container holding nanoparticles having at least a first type of oligonucleotides attached thereto, the first type of oligonucleotides having a hydrophobic group attached to the end not attached to the nanoparticles.

77. The kit of Claim 76 wherein:

the nanoparticles in the second container have a second type of oligonucleotides attached thereto, the second type of oligonucleotides having a sequence complementary to the sequence of the oligonucleotides on a second type of nanoparticles;

and the kit further comprises:

a third container holding a second type of nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to at least a portion of the sequence of the second type of oligonucleotides on the first type of nanoparticles.

78. A kit comprising at least two containers,

the first container holding particles having oligonucleotides attached thereto which have a sequence

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complementary to the sequence of a first portion of a nucleic acid, the oligonucleotides being labeled with an energy donor on the ends not attached to the particles, the second container holding particles having oligonucleotides attached thereto which have a sequence complementary to the sequence of a second portion of a nucleic acid, the oligonucleotides being labeled with an energy acceptor on the ends not attached to the particles.

79. The kit of Claim 78 wherein the energy donor and acceptor are fluorescent molecules.

80. A kit comprising at least one container, the container holding a first type of particles having oligonucleotides attached thereto which have a sequence complementary to the sequence of a first portion of a nucleic acid, the oligonucleotides being labeled with an energy donor on the ends not attached to the particles, and a second type of particles having oligonucleotides attached thereto which have a sequence complementary to the sequence of a second portion of a nucleic acid, the oligonucleotides being labeled with an energy acceptor on the ends not attached to the particles.

81. The kit of Claim 80 wherein the energy donor and acceptor are fluorescent molecules.

82. A kit comprising:



a second container holding a type of gold nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a second portion of the sequence of the nucleic acid.

84. A kit comprising:

a first container holding a first type of metallic or semiconductor nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of a nucleic acid and being labeled with a fluorescent molecule; and

a second container holding a second type of metallic or semiconductor nanoparticles having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a second portion of the sequence of a nucleic acid and being labeled with a fluorescent molecule.

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86. A kit comprising a container holding a satellite probe, the satellite probe comprising:

a particle having attached thereto oligonucleotides, the oligonucleotides having a first portion and a second portion, both portions having sequences complementary to portions of the sequence of a nucleic acid; and

probe oligonucleotides hybridized to the oligonucleotides attached to the nanoparticles, the probe oligonucleotides having a first portion and a second portion, the first portion having a sequence complementary to the sequence of the first portion of the oligonucleotides attached to the particles, both portions having sequences complementary to portions of the sequence of the nucleic acid, the probe oligonucleotides further having a reporter molecule attached to one end.

87. A substrate having nanoparticles attached thereto.

88. The substrate of Claim 87 wherein the nanoparticles have oligonucleotides attached thereto which have a sequence complementary to the sequence of a first portion of a nucleic acid.

89. A metallic or semiconductor nanoparticle having oligonucleotides attached thereto, the oligonucleotides being labeled with fluorescent molecules at the ends not attached to the nanoparticle.

90. A satellite probe comprising:

a particle having attached thereto oligonucleotides, the oligonucleotides having a first portion and a second portion, both portions having sequences complementary to portions of the sequence of a nucleic acid; and

probe oligonucleotides hybridized to the oligonucleotides attached to the nanoparticles, the probe oligonucleotides having a first portion and a second portion, the first portion having a sequence complementary to the sequence of the first portion of the oligonucleotides attached to the particles, both portions having sequences complementary to portions of the sequence of the nucleic acid, the probe oligonucleotides further having a reporter molecule attached to one end.

91. A method of nanofabrication comprising

providing at least one type of linking oligonucleotide having a selected sequence, the sequence of each type of linking oligonucleotide having at least two portions;

providing one or more types of nanoparticles having oligonucleotides attached thereto, the oligonucleotides on each of the types of nanoparticles having a sequence complementary to the sequence of a portion of a linking oligonucleotide; and

contacting the linking oligonucleotides and nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles

92. The method of Claim 91 wherein the nanoparticles are made of gold.

93. The method of Claim 91 wherein at least two types of nanoparticles having oligonucleotides attached thereto are provided, the oligonucleotides on the first type of nanoparticles having a sequence complementary to a first portion of the sequence of a linking oligonucleotide, and the oligonucleotides on the second type of nanoparticles having a sequence complementary to a second portion of the sequence of the linking oligonucleotide.

94. The method of Claim 93 wherein the nanoparticles are made of gold.

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contacting the first and second types of nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles to each other so that a desired nanomaterial or nanostructure is formed.

96. The method of Claim 95 wherein the nanoparticles are made of gold.

97. Nanomaterials or nanostructures composed of nanoparticles having oligonucleotides attached thereto, the nanoparticles being held together by oligonucleotide connectors.

98. The nanomaterials or nanostructures of Claim 97 wherein at least some of the oligonucleotide connectors are triple-stranded.

99. The nanomaterials or nanostructures of Claim 97 wherein the nanoparticles are made of gold.

100. A composition comprising at least two types of nanoparticles having oligonucleotides attached thereto, the oligonucleotides on the first type of nanoparticles having a sequence complementary to the sequence of a first portion of a nucleic acid or a linking oligonucleotide, the oligonucleotides on the second type of nanoparticles having a sequence complementary to the sequence of a second portion of the nucleic acid or linking oligonucleotide.

101. The composition of Claim 100 wherein the nanoparticles are made of gold.

102. An assembly of containers comprising:

a first container holding nanoparticles having oligonucleotides attached thereto, and

a second container holding nanoparticles having oligonucleotides attached thereto,

the oligonucleotides attached to the nanoparticles in the first container having a sequence complementary to that of the oligonucleotides attached to the nanoparticles in the second container,

the oligonucleotides attached to the nanoparticles in the second container having a sequence complementary to that of the oligonucleotides attached to the nanoparticles in the second container.

103. The assembly of Claim 102 wherein the nanoparticles are made of gold.

104. A nanoparticle having a plurality of different oligonucleotides attached thereto.

105. A method of separating a selected nucleic acid having at least two portions from other nucleic acids, the method comprising:

providing two or more types of nanoparticles having oligonucleotides attached thereto, the oligonucleotides on each of the types of nanoparticles

having a sequence complementary to the sequence of one of the portions of the selected nucleic acid; and

contacting the nucleic acids and nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the selected nucleic acid so that the nanoparticles hybridized to the selected nucleic acid aggregate and precipitate.

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